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Thinking Longitudinally in a Cross-sectional World

Asbestos exposure is widely recognized to cause serious and often deadly health effects (1). The World Health Organization and the International Labour Organization have called for asbestos bans worldwide, and more than 40 countries have either banned or severely restricted asbestos use (2, 3). The U.S. Congress is currently considering legislation entitled the "Ban Asbestos in America Act of 2007" (4). In this issue of the *Journal* (pp. 630–637), Rohs and colleagues report dose-dependent pleural changes identified in a cross-sectional follow-up study of a cohort of workers exposed to asbestos-contaminated vermiculite originating in Libby, Montana (5). The study has particular relevance to current national and international efforts to control risk from exposure to durable fibers.

Vermiculite is a mineral that expands when rapidly heated. Expanded vermiculite is used in both industrial and consumer products, such as loose-fill attic insulation, gardening and agricultural products, and automobile brakes. Between 1925 and 1990, the majority of the world's vermiculite was mined in Libby, Montana. Amphibole minerals, including tremolite asbestos, contaminated the Libby vermiculite products (6).

In 1980, following reports of bloody pleural effusions at one industrial site, Lockey and colleagues examined 513 workers exposed to Libby vermiculite; 2.2% showed radiographic evidence of either interstitial fibrosis or pleural changes consistent with asbestos effects (7). This was an important finding at the time, especially since exposure to vermiculite had been thought by many to be essentially benign and knowledge of the contamination of Libby vermiculite was limited. The Rohs and colleagues' study examines the same cohort of workers 25 years later. The proportion of affected workers has risen to 28.7% for pleural changes and 2.9% for fibrosis, despite no known interim exposure to asbestos. These findings are consistent with the well-known capability of asbestos to cause both malignant and nonmalignant changes years after an original exposure—effects that increase as residence time of the inhaled, biopersistent fibers lengthens (1).

The current study makes important new contributions to our understanding of the consequences of exposure to durable fibers. The investigators estimated cumulative fiber exposures for each worker based on job history and historical records of plant industrial hygiene evaluations. As expected, workers with the most exposure had the greatest probability of pleural abnormalities. What is striking, however, is the level of adverse effects in the low-exposed group: 13.9% of workers with cumulative exposures estimated between 0.25 and 0.74 fibers/cc-years showed pleural abnormalities. This compares with a current legal permissible exposure limit (PEL) in the United States that limits asbestos exposures to 0.45 fibers/cc-years over a 45-year working lifetime (8), indicating that a significant number of workers exposed at the current exposure limit would experience pleural abnormalities. Although arguments persist about the extent to which pleural abnormalities are inherently harmful, it is clear that the presence of pleural changes demonstrates a physiologic response to durable fibers and is associated with increased risk of pulmonary fibrosis, lung cancer, and mesothelioma (1).

A notable aspect of this study is the contemporary classification of the fibers contaminating the Libby vermiculite. In 1980, these fibers were classified as "tremolite asbestos" and, as such, fit within the definition of regulated asbestos fibers (8). (U.S. regulations define asbestos as one of six specific mineral fibers that are or have been of commercial value.) The current study notes that the primary durable fibers contaminating the vermiculite are winchite and richterite with perhaps 10% tremolite asbestos; however, winchite and richterite are not explicitly regulated as asbestos. This investigation does not prove that the health effects of these fibers are identical to tremolite; however, their chemical and physical properties are virtually identical to tremolite, indicating the importance of evaluating potentially harmful fibers not only on whether they meet a mineralogical definition of asbestos but also on their biologically relevant features of durability, biopersistence, shape, size, and surface characteristics. The Ban Asbestos Act explicitly expands the definition of asbestos to include winchite and richterite (4). The U.S. National Institute for Occupational Safety and Health has circulated a draft "Roadmap for Scientific Research" proposing studies that would be useful in better understanding the nature of hazardous fibers (9).

The increase in fiber-related disease from exposure to the contaminated vermiculite is not limited to the group of industrial workers examined recently by Rohs and colleagues and previously by Lockey and coworkers. Following the original report by Lockey and colleagues, investigators studied the morbidity and mortality of vermiculite miners and millers in Libby, Montana, and found increased risk of lung cancer and nonmalignant respiratory disease (10, 11). Consistent with the Rohs report, a recent update of that cohort mortality study confirmed significant excess deaths from asbestosis, lung cancer, cancer of the pleura, and mesothelioma at fiber exposure levels lower than in the original study (12).

These findings, as a whole, highlight the importance of interpreting and responding to cross-sectional research findings not only according to what they say about the present but also in the context of what they indicate about the future. The initial Lockey investigation found a relatively modest 2.2% prevalence of pleural abnormalities; Rohs and colleagues found over 10 times that level, despite the fact that contaminated vermiculite had been removed from the production process by 1980. In Libby, Montana, miners and millers continued to be exposed to the contaminated vermiculite until mining operations ceased in 1990, and their current mortality experience, after continuing exposure and longer latency, reflects this as well (12). Consumers of vermiculite originating in Libby have also been exposed to potentially hazardous fibers (13).

Anticipation of potential risk is the keystone of occupational disease and injury prevention (14). Had the early cross-sectional investigations of disease from contaminated vermiculate stimulated assessment of future risk, it is possible that the number of people exposed to hazardous fibers, their level of exposure, and disease risk could have been reduced.

The opportunity for prevention of fiber-related morbidity and mortality remains. Recent investigations have demonstrated strong relationships between national asbestos consumption rates and levels of asbestos-associated mortality after a lengthy lag (15). Although the United States has successfully restricted asbestos exposure and is considering a ban, consumption in some countries with rapidly developing economies is continuing to expand (16). Bans and effective use restrictions worldwide have the potential to prevent decades of future death and disease.

Wayne Gretzky, an exceptional ice hockey player, famously attributed his athletic accomplishments to the ability to "skate to where the puck is going to be." Through more effective response to cross-sectional scientific findings based on understanding their future implications, particularly for long-latency diseases, the medical and public health communities have the opportunity to emulate Gretzky's success.

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